Patent
Attorney's Docket No. 012712-105

IN THE EUROPEAN PATENT OFFICE

In re Patent Application of)
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IDEC Pharmaceuticals Corp.)
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Application No.: 94901444.3)
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Filed: June 9, 1995)
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For: THERAPEUTIC APPLICATION OF)
CHIMERIC AND RADIOLABELED)
ANTIBODIES TO HUMAN B LYMPHO-)
CYTE RESTRICTED DIFFERENTI-)
ATION ANTIGEN FOR TREATMENT...)

DECLARATION OF DARRELL R. ANDERSON

The European Patent Office
P B 5818 Patentlaan 2
2280 HV Rijswijk (ZH)
Netherlands

Sir:

I, Darrell R. Anderson, declare and state as follows:

(1) I reside at 1851 Navajo Place, Escondido, California 92029.

(2) I am the same Darrell R. Anderson who is an inventor on the above-identified application. I am also the same Darrell R. Anderson who is an author on "Immunoreactivity and Effector Function Associated with a Chimeric Anti-CD20 Antibody," Anderson et al, *The 2nd Annual IBC International Conference on Antibody Engineering* (December 16-18, 1991 (hereinafter "the Anderson abstract" or "the Anderson reference").

(3) The Anderson reference is an abstract which was presented at the IBC International Conference. This abstract generally relates to the C2B8 and the 2B8 antibodies. More particularly, and as reflected by the title of the abstract, the Anderson reference

relates to the immunoreactivity and effector functions associated with the C2B8 antibody. The abstract further describes that the C2B8 antibody is a chimeric antibody containing human constant regions and murine variable regions which binds to the human CD20 antigen. The abstract further discloses that the 2B8 antibody is the murine anti-CD20 antibody from which the variable regions contained in the C2B8 antibody were derived. Also, the Anderson abstract contains information relating to the potential usage of the C2B8 antibody for the treatment for B cell lymphoma.

(4) However, as discussed in the letter submitted to the European Patent Office on September 5, 1995, the Anderson abstract does not contain sufficient information to enable one skilled in the art to synthesize or otherwise obtain the C2B8 or the 2B8 antibodies. For example, this abstract does not contain any amino acid or DNA sequence information relating to the C2B8 or the 2B8 antibody. Moreover, no amino acid or DNA sequence information relating to either the C2B8 or the 2B8 antibody was reported in the literature or otherwise publicly disseminated prior to the November 13, 1992 priority date of this application. Furthermore, neither the C2B8 antibody or the 2B8 antibody, or cell lines which produce either of these antibodies were made publicly available prior to the November 13, 1992 priority date of this application.

The undersigned inventor declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false

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statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

Date: 2/1/96

Darrell R. Anderson

Darrell R. Anderson, PhD.

Press Release

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RLT

FOR IMMEDIATE RELEASE

IDEC PHARMACEUTICALS UPDATES LYMPHOMA TRIAL RESULTS FOR IDEC-C2B8, BOTH AS SINGLE AGENT AND IN COMBINATION WITH CHEMOTHERAPY

AMSTERDAM, NETHERLANDS (March 13, 1996): IDEC Pharmaceuticals Corp. (Nasdaq: IDPH) of San Diego, CA today updated its clinical experience with IDEC-C2B8 for treatment of non-Hodgkin's B-cell lymphomas at the 9th National Cancer Institute-EORTC Symposium on New Drugs and Cancer Therapy held in this city. The Company's presentations featured updates of results from an ongoing Phase II combination trial of IDEC-C2B8 and CHOP chemotherapy, and a follow-up report of a completed Phase II study of IDEC-C2B8 used as a single agent. In the ongoing combination therapy trial, all of the patients treated to date have responded (100% overall response rate), and 28 out of 29 responses are ongoing from six to 22 months. Of the 29 patients completing all scheduled treatments, 19 (66%) have achieved a complete response and 10 (34%) have achieved a partial response. Moreover, six of seven patients, who prior to treatment expressed a cellular marker associated with malignant cells called bcl-2, became negative for that marker as detected by sensitive PCR assay by the completion of therapy.

"IDEC-C2B8 appears to work by different mechanisms from chemotherapy and sensitizes drug-resistant human cell lines to chemotherapeutic agents," said IDEC senior vice president of medical and regulatory affairs, Antonio J. Grillo-López, M.D. "Moreover, the antibody exhibits therapeutic activity on its own, producing only limited toxicity that does not overlap with the toxicities produced by chemotherapy. As a result, IDEC-C2B8 offers potential both as a single agent therapeutic for B-cell lymphomas and in combination with chemotherapy."

The planned enrollment of 40 patients has been completed in IDEC's ongoing Phase II combination trial of IDEC-C2B8 and CHOP. In this trial, patients with low grade or follicular lymphoma receive six doses of IDEC-C2B8 over 21 weeks. Within this same time period, they also receive six cycles of CHOP chemotherapy (a standard regimen of cyclophosphamide, doxorubicin, vincristine and prednisone). Patients have tolerated the combination of IDEC-C2B8 and CHOP well, as adverse events do not appear to exceed those expected with CHOP alone. IDEC expects to complete patient treatment and to have the final results from this trial by the end of the year.

"We have continued to see conversions from bcl-2 positive to bcl-2 negative in patients whose status was known prior to treatment, whereas patients treated with conventional chemotherapy alone generally do not become bcl-2 negative," commented Dr. Grillo-López. The bcl-2 gene often has undergone a change in chromosomal location in individuals with follicular or low grade lymphomas. Thus, for patients with lymphoma, bcl-2 status post-therapy may have prognostic value and may also serve as a marker to monitor minimal, residual disease.

IDEC Pharmaceuticals today also updated its now completed Phase II trial of IDEC-C2B8 as a single agent for treatment of low grade or follicular lymphomas. In this trial, 17 of 34 (50%) evaluable patients experienced a complete or partial response (i.e. tumor shrinkage of 50% or greater) after receiving four weekly infusions of the antibody. Patients tolerated treatment well on an outpatient basis, and treatment with IDEC-C2B8 did not preclude subsequent chemotherapy or show any adverse effect on marrow reserve. Despite the brief treatment period with IDEC-C2B8, five patients in this trial had tumor remissions lasting greater than 20 months; four of these have tumor remissions which continue without maintenance therapy at 20.6+, 22.1+, 22.5+ and 23.4+ months.

IDEC is developing IDEC-C2B8 in collaboration with Genentech, Inc. and Zenyaku Kogyo Co. Ltd. IDEC Pharmaceuticals recently announced the completion of patient accrual in an open label, pivotal, Phase III trial of IDEC-C2B8 as a single agent treatment for low grade and follicular non-Hodgkin's lymphomas. Final results of the 150-patient trial are not anticipated until late 1996, to allow for patient follow-up and audit of clinical data.

B-cell lymphomas are usually fatal malignancies of the body's antibody-producing cells. Non-Hodgkin's lymphomas currently afflict roughly 225,000 Americans, with over 50,000 new

diagnoses expected this year. Low grade and follicular lymphomas comprise about sixty-five percent (65%) of the total lymphoma prevalence in the U.S.

IDEC Pharmaceuticals focuses on developing targeted immunotherapies for the treatment of cancer and autoimmune diseases. IDEC's products are primarily designed to act through immune mechanisms and potentially offer greater specificity of action, longer therapeutic effect and lower toxicity than is typical of existing therapies. All of IDEC's products are designed for administration in outpatient settings, providing the opportunity to reduce overall treatment costs.

IDEC Pharmaceuticals' press releases are available at no charge through PR Newswire's "Company News On-Call" fax service. For a menu of IDEC's current press releases and quarterly reports or to retrieve a specific release, call (800) 758-5804, ext. 432581 or internet http://www.prnewswire.com.

The statements made in this press release contain certain forward looking statements that involve a number of risks and uncertainties. Actual events or results may differ from the Company's expectations. In addition to the matters described in this press release, timelines for clinical ongoing activity are subject to change, results of pending or future clinical trials cannot be accurately predicted, and decisions by the FDA and other regulatory agencies, as well as the risk factors listed from time to time in the Company's SEC reports, including but not limited to its report on Form 10-Q for the quarter ended September 30, 1995 as well as its Annual Reports on Form 10-K, may affect the actual results achieved by the Company.

IDEC Pharmaceuticals® is a registered U.S. trademark of the Company. The Company is located at 11011 Torreyana Road, San Diego, CA 92121.